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Are Conventional Combined Training Interventions and Exergames Two Facets of the Same Coin to Improve Brain and Cognition in Healthy Older Adults? Data-Based Viewpoint

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Abstract

Combining physical, motor, and cognitive exercises is expected to be effective to attenuate age-related declines of brain and cognition in older adults. This can be achieved either by conventional interventions or by exergames. This paper aimed to determine whether conventional combined training and exergame interventions are two comparable ways for delivering combined training. In total, 24 studies on conventional training and 23 studies on exergames were selected and compared. A common framework was used to analyze both types of combined training interventions. Our analysis showed that conventional combined training interventions were more effective than separated physical and motor training to improve brain and cognition, while their superiority over cognitive training alone remains to be confirmed. Exergames scarcely led to cognitive benefits superior to those observed after physical, motor, or cognitive training alone. Thus, although both conventional training interventions and exergames allowed delivering combined training programs, they are not two facets of the same coin. Further studies that are more theoretically grounded are necessary to determine whether interventions delivered via exergames may lead to superior benefits compared to conventional separated and combined training interventions.

Introduction

Delaying or attenuating age-related cognitive decline is critical for preserving autonomy and quality of life of the increasing number of older adults. It has been widely demonstrated that separate cognitive, aerobic, muscular, and motor training are effective in this respect [1]. Moreover, it has been suggested that their integration into combined training interventions (CTIs) might be more effective than separated training [2-4]. In this context and in view of the role played by cognitive stimulations in CTIs [5,6], exergames (ie, interactive video games that require participants to be physically active to play) might be even more effective than conventional combined training programs, since they conjugate the effects of physical and motor exercises [1,7] and those of video game training on cognitive performance [8,9]. However, until now, no study has systematically compared, within the same experimental protocols, the respective benefits of ‘conventional’ CTIs and exergames with regard to cognitive outcomes in healthy older adults. "A review of reviews" (ie, 3 reviews on conventional cognitive and motor training and 3 on exergames) [10] recently addressed this issue and reported conflicting results. Specifically, the benefits of conventional CTIs were found superior to those of separated training in 2 reviews, but the superiority of exergames over
This paper aims to go a step further by reporting the results of a detailed comparison of studies that used conventional CTIs and those that used exergames to improve brain and cognition in healthy older adults. To fulfill this objective, based on the framework developed in 2 recently published review papers dedicated to conventional CTIs [11] and exergames [12], we compiled the data of 47 studies to compare randomized controlled trials and controlled trials that have used either conventional combined training or exergames to improve cognitive functions (Table 1 and Table 2).

**Table 1.** Selected reviews and studies on conventional combined training interventions. Studies were classified as a function of the type of combined intervention.

<table>
<thead>
<tr>
<th>Conventional combined training interventions</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reviews</td>
<td>Law et al [13], Wollesen and Voelcker-Rehage [14], Zhu et al [15], Lauenroth et al [3], Levin et al [16], Tait et al [17], Gheysen et al [2], Joubert and Chainay [18], Gavelin et al [19], Wollesen et al [20], Gallou et al [10], Gou et al [21]</td>
</tr>
<tr>
<td>Studies Sequential</td>
<td></td>
</tr>
<tr>
<td>PCT</td>
<td>Fabre et al [22], Legault et al [23]</td>
</tr>
<tr>
<td>MCT</td>
<td>Oswald et al [29]</td>
</tr>
<tr>
<td>MDT</td>
<td>Pieramico et al [30], Van het Reve and de Bruin [31], Rahe et al [32], Rahe et al [33], Kalbe et al [34]</td>
</tr>
<tr>
<td>Simultaneous</td>
<td></td>
</tr>
<tr>
<td>PCT</td>
<td>Theill et al [35], Leon et al [36], Norouzi et al [37], Eggenberger et al [38], Eggenberger et al [39]</td>
</tr>
<tr>
<td>MCT</td>
<td>Hiyamizu et al [40], Marmeleira et al [41], Falbo et al [42]</td>
</tr>
<tr>
<td>MDT</td>
<td>Ansai et al [43], Yokoyama et al [44], Nishiguchi et al [45], Jardim et al [46]</td>
</tr>
</tbody>
</table>

*PCT: physical-cognitive training.
*MCT: motor-cognitive training.
*MDT: multidomain training.

**Table 2.** Selected reviews and studies on exergames. Studies were classified as a function of the type of combined intervention.

<table>
<thead>
<tr>
<th>Exergames interventions</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reviews</td>
<td>Zhang and Kaufman [47], Bleakley et al [48], Ogawa et al [49], Howes et al [50], Stanmore et al [51], Vázquez et al [52], Mansor et al [53], Stojan and Voelcker-Rehage [54], Gallou-Guyot et al [10], Wollesen et al [20], Gavelin et al [19], Sakaki et al [55], Soares et al [56]</td>
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<tr>
<td>Studies</td>
<td></td>
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<tr>
<td>Sequential</td>
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<td>PCT</td>
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<tr>
<td>MCT</td>
<td>Park and Yim [57]</td>
</tr>
<tr>
<td>MDT</td>
<td>Kayama et al [58]</td>
</tr>
<tr>
<td>Simultaneous</td>
<td></td>
</tr>
<tr>
<td>PCT</td>
<td>Anderson-Hanley et al [59], Barcelos et al [60]</td>
</tr>
<tr>
<td>MCT</td>
<td>Schoene et al [61], Schoene et al [62], Gschwind et al [63], Schättin et al [64], Adcock et al [65], Carrasco et al [66], Eggenberger et al [39], Eggenberger et al [67], Huang [68], Li et al [69]</td>
</tr>
<tr>
<td>MDT</td>
<td>Maillet et al [70], Chuang et al [71], Ordnung et al [72], Guimaraes et al [73], Hrut et al [74], Bacha et al [75], Peng et al [76], Moreira et al [77], Gouveia et al [78]</td>
</tr>
</tbody>
</table>

*PCT: physical-cognitive training.
*Not available.
*MCT: motor-cognitive training.
*MDT: multidomain training.
A Structured Framework for Analyzing Combined Training Interventions

We developed a framework to analyze CTIs, independent of whether they were delivered via conventional interventions or via exergames. Specifically, we distinguished the following: (1) the stimuli, which refer to different types of combined training; (2) the settings, which are the organizing features of training programs (ie, frequency, duration, intensity, instructions, feedback, individualization, and progressivity of increase in difficulty); (3) the targets of training, which were limited in this review to brain and cognitive levels, but other levels could be added in future works; (4) the markers, that is, the tasks and tests used to train or assess the participants, respectively; (5) the outcomes of different types of training, that is, the different variables that allow for quantifying the observed effects at brain and cognitive levels; (6) the moderators, who modulated the effects of training; and (7) the potential mechanisms, which were explicitly mentioned in different studies to predict and explain the effects of combined training (Figure 1).

Accordingly, 3 main training modes were distinguished: (1) physical-cognitive training (PCT), which correspond to the association of endurance (aerobic) and muscular resistance training and cognitive training, either sequentially or simultaneously; (2) motor-cognitive training (MCT), which refers to the association of complex motor skills training and cognitive training, implemented through the addition of cognitive tasks separated from the motor tasks (eg, mental calculation); and (3) multidomain training (MDT), which consists of associating aerobic exercises, complex motor skills, and cognitive tasks through laboratory-customized training situations. Notably, for conventional CTIs, we limited our analysis to randomized controlled trials and controlled trials in which it was possible to identify different training components (ie, physical, motor, and cognitive) that were associated with each other. Thus, according to this criterion, interventions implemented through natural motor activities (eg, tai chi, dance, or Nordic walking) were excluded. Although these activities included physical, motor, and cognitive components, their respective weights and levels of intensity or complexity were difficult to quantify. Based on this framework, in this study, we focused our comparative analysis on the following 4 main constructs: stimuli, settings, targets, and outcomes.

Figure 1. A multidimensional framework to analyze combined training interventions (detailed explanations are presented in a previous study [11]). Published under Creative Commons Attribution 4.0 International License.
The Database

Our analysis was grounded on the material included in 2 recently published reviews dedicated to conventional CTIs [11] and exergames [12], respectively. Specifically, 24 studies on conventional training and 23 studies on exergames, published from 2010 to November 2021, were selected on the basis of several criteria [11,12]. These studies were then analyzed to compare them according to the 4 chosen constructs of our framework (Table 1 and Table 2).

Quantitative and Qualitative Differences Between Conventional Interventions and Exergames

Stimuli

Motor and cognitive exercises were performed simultaneously in 100% (n=23) of the exergames studies, whereas sequential presentation of physical and cognitive exercises was used in 58% (7/12) of conventional PCT studies, 22% (2/9) of MDT studies, and 50% (2/4) of MCT studies. Thus, one can hypothesize that several studies on conventional CTIs used mechanisms that were different from those involved in exergame interventions. Another important issue concerns the distribution of the 3 training modes (ie, PCT, MCT, and MDT), which differed in conventional CTI and exergames studies. Indeed, the proportion of PCT studies was much higher for conventional interventions compared to exergaming (12/24, 50% and 2/23, 8%, respectively), whereas the inverse was observed for MCT 16% (4/24) for conventional interventions and 47% (11/23) for exergaming, respectively) and MDT studies 37% (9/24) for conventional studies and 43% (10/23) for exergaming, respectively. This resulted from the predominant use of commercial exergames (eg, Xbox Kinect and Wii Balance Board), which were cheaper than the stationary cybercycle used for implementing PCT in exergames studies [59,60]. It could be concluded from the distribution of PCT in both conventional and exergaming intervention studies that, on average, the latter was less physically demanding than the former; supporting evidence could be found in a study by Graves et al [79], and a discussion is presented in Gonçalves et al’s 2021 study [80]. However, this issue is a matter of debate, since few studies demonstrated that commercial exergames can be the support of intense physical activity [81,82], whereas others showed that they only facilitated light- to moderate-intensity physical activity [83]. On the other hand, since commercial exergames usually required upper limb movements, whole body movements, stepping, weight shifting or balance control, motor exercises supporting MCT and MDT in conventional CTIs and exergames studies were roughly similar.

Settings

Conventional CTIs most frequently aimed to compare several groups simultaneously. Indeed, 21/24 (87%) involved a passive control group, alone or together with cognitive training (15/24, 62%) and physical or motor training (13/24, 54%) groups. In total, 8/24 (33%) of the conventional training studies involved 3 training groups (ie, CTI, physical or motor, and cognitive), whereas it was the case in only 1/23 (4.3%) of the exergames studies. Most frequently, exergames studies included 2 groups, that is, either a passive control group (9/23, 39.1%), a physical or motor training group (13/24, 56.5%), or less frequently, a cognitive training group (2/23, 8.6%), in addition to the exergaming group. In both conventional CTI and exergames studies, permanence and transfer of training effects were scarcely investigated, so no reliable conclusion can be drawn in this respect.

Targets

No main difference was observed between the cognitive abilities tested in conventional CTIs and exergames studies. The most frequently tested were memory, executive functions, attention, and information processing speed, but there were no ‘a priori’ assumptions about the type of functions that could be affected more or less by each CTI. The respective effects of conventional combined training and exergames on brain health and neurobiological mechanisms cannot be reliably compared due to the small number of related studies and their heterogeneity (ie, 4 and 2 studies, respectively).

Outcomes

Combined Training Versus Passive Control Groups

Independent of the training modes (ie, PCT, MCT, or MDT), positive effects were observed, relative to passive control groups, in all conventional CTIs and exergames studies, for at least one of the targeted cognitive functions, that is, memory, attention, executive functions, and information processing speed. These results were observed for both sequential and simultaneous associations between cognitive and physical or motor exercises. Unfortunately, it was impossible to determine whether cognitive functions were differently impacted by conventional combined training and exergames, respectively. These results are consistent with those reported by Gallou-Guyot et al [10]. Unsurprisingly, they suggest that regardless of how combined training is delivered (ie, conventional interventions or exergames, and PCT, MCT, or MDT), combined training programs always lead to superior benefits compared to inactivity.

Combined Training Versus Physical Training

In conventional CTIs, superior benefits of combined training over separated physical training were observed in 100% (n=13) of MCT and MDT studies and in most of the PCT studies (8/12, 66.6%). On the other hand, superior benefits of exergaming compared to conventional physical or motor training alone were observed in only one study on exergames [59], whereas no difference was found between the exergames and separated training groups in the 4 other studies (2 on MCT and 2 on MDT).

Combined Training Versus Cognitive Training

In conventional training studies, compared to cognitive training alone, superior benefits of CTIs were observed in almost one-third of PCT studies (n=4), but never in MCT and MDT studies. In the 2 studies that compared exergaming and cognitive training, one reported a superiority of the former over the latter on executive functions [67], whereas the other did not [74].
Thus, the number of related studies was too small to draw reliable conclusions about the superiority of exergames over cognitive training alone.

Limitations and Study Comparisons

The studies including 4 training groups (ie, combined training, separated physical and cognitive training, and a control group), which could allow for a complete comparison, were scarce (ie, 8 conventional training studies out of 47, in total). A second observation was that despite the type of intervention (ie, conventional or exergames), the mechanisms underlying eventual differences with physical and cognitive training groups were rarely addressed in the reviewed studies. A third observation was that information relative to intensity and the nature of physical exercises, the nature and levels of complexity of motor exercises, and progressivity of difficulty was neglected in most studies, so it was impossible to estimate why physical or motor training was effective (or not) to improve physical, motor, or cognitive performance. This was the case, in particular, in exergames studies. In addition, in several studies, cognitive training procedures and (exer)game contents were not described or were only superficially described. Finally, due to the small number of studies available to support some comparisons (eg, exergames and cognitive training; conventional CTI vs exergames), the results remain to be confirmed or even established in future studies.

Discussion

In this paper, we aimed to determine whether conventional CTIs and exergames were two comparable ways for delivering combined training. Our analysis showed that conventional CTIs were more effective than separated physical and motor training to improve brain and cognition, but their superiority over cognitive training alone remains to be confirmed in further studies. On the other hand, exergames scarcely led to cognitive benefits superior to those observed after physical, motor, or cognitive training alone. A plausible reason is that the existing exergames did not allow reaching high enough levels of physical effort [10] or motor skills complexity, and they used the resources of virtual reality and video games insufficiently to improve the cognitive load of different exercises [84]. This is not to say that exergame interventions cannot succeed in being more effective than conventional CTIs. However, further studies, grounded on theoretical knowledge provided by the literature on physical, motor, and cognitive training are necessary to determine whether interventions delivered via exergames may lead to superior benefits compared to separated and combined CTIs. In particular, since commercial exergames are not designed specifically for older adults, exergames studies should use new solutions that are more grounded on theoretical foundations [84].

Finally, this analysis showed that conventional CTIs and exergames studies did not address the same research questions, thereby precluding reliable comparisons of their benefits. Specifically, conventional CTI studies prominently aimed to compare benefits of separate training programs, whereas exergames studies focused on the benefits of exergaming per se, most often relative to inactive control groups. Thus, contrarily to our expectations, they seem to be separated domains of the literature on aging, which, until now, have developed independently of each other. In particular, the literature on exergames has not yet reached the level of maturity of those on conventional CTIs, which itself remains heterogeneous and suffers from methodological weakness and lack of a strong conceptual background [11,84,85]. Therefore, although they both allow for delivering combined training programs, conventional and exergames interventions are not two facets of the same coin; rather, they are two coins we do not know which is more valuable. Accordingly, future studies should aim to develop new exergames that would capitalize more on the knowledge from studies on conventional CTIs, particularly concerning the underlying mechanisms. These studies should also systematically compare the effectiveness of existing or new exergames and that of conventional CTIs.

Conflicts of Interest

None declared.

References


Abbreviations

CTI: combined training intervention
MCT: motor-cognitive training
MDT: multidomain training
**PCT**: physical-cognitive training
Effects of Cybersickness Caused by Head-Mounted Display–Based Virtual Reality on Physiological Responses: Cross-sectional Study

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Abstract

Background: Although more people are experiencing cybersickness due to the popularization of virtual reality (VR), no official standard for the cause and reduction of cybersickness exists to date. One of the main reasons is that an objective method to assess cybersickness has not been established. To resolve this, research on evaluating cybersickness with physiological responses that can be measured in real time is required. Since research on deriving physiological responses that can assess cybersickness is at an early stage, further studies examining various physiological responses are needed.

Objective: This study analyzed the effects of cybersickness caused by head-mounted display–based VR on physiological responses.

Methods: We developed content that provided users with a first-person view of an aircraft that moved (with translation and combined rotation) over a city via a predetermined trajectory. In the experiment, cybersickness and the physiological responses of participants were measured. Cybersickness was assessed by the Simulator Sickness Questionnaire (SSQ). The measured physiological responses were heart rate, blood pressure, body temperature, and cortisol level.

Results: Our measurement confirmed that all SSQ scores increased significantly (all $P$s<.05) when participants experienced cybersickness. Heart rate and cortisol level increased significantly ($P=.01$ and $P=.001$, respectively). Body temperature also increased, but there was no statistically significant difference ($P=.02$). Systolic blood pressure and diastolic blood pressure decreased significantly ($P=.001$).

Conclusions: Based on the results of our analysis, the following conclusions were drawn: (1) cybersickness causes significant disorientation, and research on this topic should focus on factors that affect disorientation; and (2) the physiological responses that are suitable for measuring cybersickness are heart rate and cortisol level.

(JMIR Serious Games 2022;10(4):e37938) doi:10.2196/37938

KEYWORDS

cybersickness; physiological responses; virtual reality; VR; head-mounted displays; heart rate; cortisol
**Introduction**

The recent development of technologies such as head-mounted displays (HMDs) and motion-tracking devices has enabled active research on virtual reality (VR). VR is used in various fields, such as in games, education, medicine, and health care [1]. Although VR can improve the user's concentration by providing an immersive experience, some users may experience cybersickness, which is a type of motion sickness [2].

The most well-known theory for explaining motion sickness is the sensory conflict theory. According to the sensory conflict theory, motion sickness is caused by a discordance between the vestibular sense and the visual perception of body movement [3-6]. In addition, according to the sensory conflict theory, motion sickness is classified into motion-induced motion sickness (MIMS) and visually induced motion sickness (VIMS). MIMS is further classified according to the external environment as car, ship, and air (flight) sickness [7-10], and VIMS is further classified into simulator motion sickness and cyber motion sickness according to the display device [11,12]. Simulator motion sickness is caused in virtual training such as flying and driving [13-15], and cyber motion sickness is caused in virtual environments that are completely different from real ones [16].

Although more people are experiencing cybersickness due to the popularization of VR, no official standard for the cause and reduction of cybersickness exists to date. One of the main reasons is that an objective method to assess cybersickness has not been established. Vomiting has been used as a diagnostic criterion for motion sickness because it is difficult to assess other symptoms quantitatively [17]. However, because there are instances of motion sickness that do not accompany vomiting, the Motion Sickness Assessment Questionnaire (MSAQ) [18] and the Simulator Sickness Questionnaire (SSQ) [19] have been proposed to assess motion sickness symptoms. The MSAQ has been used extensively in traditional motion sickness studies; however, it is not suitable for VIMS assessment. The SSQ, which is optimized from the MSAQ and focuses on VIMS, is mostly used in studies assessing simulator sickness and cybersickness. Even though the SSQ is low-cost and easy to use, its objectiveness is questionable and its real-time implementation is difficult [20,21].

To solve this problem, research on evaluating cybersickness with physiological responses that can be measured in real time is required [22,23]. To assess cybersickness in terms of physiological responses, it is necessary to find out the factors that are correlated with cybersickness. Conventional studies have reported that physiological responses, such as specific frequency power bands of the electroencephalogram [24-26], gastrointestinal activity [27], heart rate [28-30], and skin conductance [31], can be used to assess cybersickness. In particular, heart rate has been reported to be related to the stress task when playing a video [29,30]. Although conventional research into cybersickness is extensive, this issue remains in the HMD-based VR context [32]. Many validation experiments are necessary to generalize these physiological responses. Since research on deriving physiological responses that can assess cybersickness is at an early stage, further research on various physiological responses is still required. Therefore, this paper deals with the effects of cybersickness caused by HMD-based VR on physiological responses.

**Methods**

**Design and Setting**

We performed an experiment where participants watched HMD-based VR content in the environment shown in Figure 1.

Conventional studies on the effect of the content itself have shown that rotational movement causes higher motion sickness than a linear one [33] and that a combined rotation of more than 1 axis causes greater motion sickness than a rotation of a single axis [34,35]. Based on those conventional studies, our HMD-based VR content was developed to intentionally cause cybersickness using Unity 3D (Unity Technologies) [36]. In addition, the longer the exposure time, the higher the level of cybersickness, so the playing time of the developed content was configured to be the least amount of time needed to measure the physiological response.

The developed content provided the user with a first-person view of an aircraft that moved (with translation and combined rotation) over a city via a predetermined trajectory.
Questionnaire, Variables, and Equipment

The SSQ [19] was used to assess cybersickness. This questionnaire consists of 16 questions with 3 subscales corresponding to symptom clusters (nausea, oculomotor symptoms, and disorientation). Each question is measured on a 4-point scale from 0 to 3 points. A total score represents the complete symptom level of motion sickness. A higher score indicates more severe motion sickness.

In an experiment conducted on a Korean population [37], it was confirmed that the SSQ significantly increased in HMD-based environments compared to screen-based environments, which suggests it could have validity and reliability in measuring cybersickness.

In an experiment conducted on a Korean population [37], it was confirmed that the SSQ significantly increased in HMD-based environments compared to screen-based environments, which suggests it could have validity and reliability in measuring cybersickness.

The occurrence of motion sickness is highly related to the autonomic nervous system [38]. Therefore, in this experiment, physiological responses related to the autonomic nervous system were measured to examine whether or not the responses related to motion sickness can be applied to HMD-based cybersickness.

We measured the following physiological responses that relate to the autonomic nervous system: heart rate, blood pressure, body temperature, and cortisol level. Blood pressure was measured as 2 values: systolic and diastolic. Systolic blood pressure indicates the highest pressure in the artery when the heart is contracted, and diastolic blood pressure indicates the lowest pressure in the artery right before the heart contracts again. Body temperature was measured with a digital thermometer. Cortisol, which is produced under stress, was measured from 4 cc of blood collected over 2 minutes with the support of a clinician at Cheonan Medical Center [39].

The HMD used in the experiment was the HTC Vive (HTC Corporation) [40]. To minimize the effect of the vestibular sense, we controlled body motion in addition to head translation and rotation.

Participants

A total of 16 undergraduate and graduate students (male: n=8, 50%; female: n=8, 50%) participated in the experiment. The participants had no history of problems associated with the nervous system, autonomic nervous system, and visual system. In addition, more than 8 hours of sleep was recommended to prevent increased cybersickness sensitivity among participants [41]. Prior to participation, we explained the experiment, apart from the objective, and then obtained written consent to participate.
Procedures

The experimental procedure consisted of 3 steps (pre-experiment, experiment, and postexperiment) as shown in Textbox 1. In the pre-experiment step, SSQ and the physiological responses of the participants were measured. In the experiment step, participants viewed the HMD-based VR content that we developed during the design phase. The participants sat and watched the VR content without moving. By making the participants concentrate only on watching the VR content, we ensured their stress level was affected solely by cybersickness.

In the postexperiment step, participants’ physiological responses and SSQ outcomes were measured. Each step was performed for 2 minutes, and the total experiment time was 10 minutes.

Textbox 1. The experimental procedure.

<table>
<thead>
<tr>
<th>Pre-experiment step</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Simulator Sickness Questionnaire (SSQ) measurement (2 minutes)</td>
</tr>
<tr>
<td>• Physiological response measurement (2 minutes)</td>
</tr>
<tr>
<td>Experiment</td>
</tr>
<tr>
<td>• Head-mounted display–based virtual reality content viewing (2 minutes)</td>
</tr>
<tr>
<td>Postexperiment step</td>
</tr>
<tr>
<td>• Physiological response measurement (2 minutes)</td>
</tr>
<tr>
<td>• SSQ measurement (2 minutes)</td>
</tr>
</tbody>
</table>

Data Analysis

We analyzed the data measured in the experiment using SPSS Statistics (version 21; IBM Corp) [42]. The data measured in the experiment were SSQ items, heart rate, body temperature, blood pressure, and cortisol. A statistical analysis (paired t test) was applied to find significant differences between the measured data in the pre- and postexperiment steps. SSQ scores from before and after the experiment were compared to detect the presence of cybersickness. If found, we analyzed how each physiological response was related to cybersickness in the HMD-based environment.

Ethics Approval

The study was approved by the institutional review board of the Korea University of Technology and Education (IRB-17122602).

Results

SSQ Analysis

The SSQ scores measured before and after the experiment are shown in Figure 2. In the pre-experiment step, the mean SSQ scores for nausea, oculomotor, disorientation, and total score were 4.17, 15.63, 5.22, and 10.75, respectively. In the postexperiment step, they were 32.79, 38.77, 64.38, and 49.32, respectively. From the measurement results, it was confirmed that all SSQ scores increased significantly, as shown in Table 1 (all Ps<.05). This indicates that cybersickness was experienced by participants viewing the HMD-based VR content.
Figure 2. The SSQ scores measured in the pre- and postexperiment steps. SSQ: Simulator Sickness Questionnaire.

Table 1. The Simulator Sickness Questionnaire scores measured before and after the experiment.

<table>
<thead>
<tr>
<th>Physiological response</th>
<th>Pre-experiment score, mean (SD)</th>
<th>Postexperiment score, mean (SD)</th>
<th>t (df)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>4.17 (6.94)</td>
<td>32.79 (34.30)</td>
<td>−3.48 (15)</td>
<td>.003a</td>
</tr>
<tr>
<td>Oculomotor</td>
<td>15.63 (16.01)</td>
<td>38.77 (24.97)</td>
<td>−3.37 (15)</td>
<td>.004a</td>
</tr>
<tr>
<td>Disorientation</td>
<td>5.22 (10.01)</td>
<td>64.38 (58.15)</td>
<td>−3.93 (15)</td>
<td>.001a</td>
</tr>
<tr>
<td>Total</td>
<td>10.75 (11.74)</td>
<td>49.32 (38.00)</td>
<td>−3.89 (15)</td>
<td>.001a</td>
</tr>
</tbody>
</table>

*aSignificant P values.

**Physiological Responses Analysis**

The physiological responses measured in the pre- and postexperiment steps are shown in Table 2. Mean heart rate before and after the experiment was 78.06 bpm and 83.50 bpm, respectively. Our measurements confirmed that heart rate increased significantly ($P = .01$; Figure 3). This means that heart rate increased when cybersickness was experienced by participants viewing the HMD-based VR content.

Table 2. Physiological responses measured before and after the experiment.

<table>
<thead>
<tr>
<th>Physiological response</th>
<th>Pre-experiment score, mean (SD)</th>
<th>Postexperiment score, mean (SD)</th>
<th>t (df)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>78.06 (7.71)</td>
<td>83.50 (10.41)</td>
<td>−2.92 (15)</td>
<td>.01a</td>
</tr>
<tr>
<td>Cortisol (ug/dl)</td>
<td>7.75 (2.62)</td>
<td>10.59 (4.12)</td>
<td>−4.72 (15)</td>
<td>.001a</td>
</tr>
<tr>
<td>Body temperature (°C)</td>
<td>37.10 (0.28)</td>
<td>37.14 (0.21)</td>
<td>−1.33 (15)</td>
<td>.20</td>
</tr>
<tr>
<td><strong>Blood pressure (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>130.81 (18.84)</td>
<td>117.31 (15.78)</td>
<td>5.43 (15)</td>
<td>.001a</td>
</tr>
<tr>
<td>Diastolic</td>
<td>76.69 (9.30)</td>
<td>67.50 (11.90)</td>
<td>4.43 (15)</td>
<td>.001a</td>
</tr>
</tbody>
</table>

*aSignificant P values.*
Figure 3. Heart rate measured in the pre- and postexperiment steps.

The mean cortisol level before and after the experiment was 7.75 ug/dl and 10.59 ug/dl, respectively. Our measurements confirmed that the cortisol level increased significantly \( (P=0.001) \) (Figure 4). This implies that the cortisol level increased when participants felt cybersickness.

Figure 4. Cortisol level measured in the pre- and postexperiment steps.

Mean body temperature before and after the experiment was 37.10 °C and 37.14 °C, respectively. As per the measurement results, body temperature increased (Figure 5), but there was no statistically significant difference \( (P=0.20) \).
Mean systolic blood pressure before and after the experiment was 130.81 mmHg and 117.31 mmHg, respectively, whereas mean diastolic blood pressure was 76.69 mmHg and 67.50 mmHg, respectively. As per the measurement results, systolic blood pressure and diastolic blood pressure decreased significantly ($P=.001$; Figure 6). This means that blood pressure decreased when cybersickness was experienced by participants.

**Discussion**

**Principal Findings**

This paper examined the effects of cybersickness on physiological responses when people watch HMD-based VR content. To this end, we performed statistical analyses of SSQ scores and physiological responses (using questionnaire responses and measurements, respectively) before and after the experiment.
SSQ scores analysis in the pre- and postexperiment steps was performed to assess whether HMD-based VR content caused cybersickness. According to previous studies assessing various motion sicknesses [21], MIMS (car, ship, and airplane), simulator sickness, and cybersickness showed the highest increase in nausea, oculomotor, and disorientation, respectively. In this study, we found the highest increase in disorientation in cases of cybersickness. This result matches that of other studies (see Table 1 and Figure 2). This indicates that when there is no vestibular stimulation caused by the movement of the body and cybersickness is caused by visual stimulation through the HMD, significant disorientation occurs. This means that there is a secondary risk of walking accidents due to disorientation as well as a primary risk of cybersickness when watching HMD-based VR content. Therefore, we believe that studies on reducing cybersickness should focus on disorientation.

Physiological responses analysis in the pre- and postexperiment steps was performed to assess physiological response due to cybersickness. Significant effects on heart rate, blood pressure, and cortisol level were found in participants experiencing cybersickness (Table 2). Heart rate and cortisol level are closely related to stress. Heart rate is explained separately by the heart-body linkage hypothesis and the heart-body dissociation hypothesis [43]. The heart-body connection hypothesis states that when a person exercises, their metabolism increases, which in turn causes their heart rate to increase. The heart-body dissociation hypothesis explains more reasonably the presence of cybersickness in a motionless state than the heart-body connection hypothesis. The heart-body dissociation hypothesis states that when a person is under stress, their metabolism increases and their heart rate increases proportionally. Conventional studies [29,30] on heart rate and stress found that participants’ heart rates increased when watching a video that was assigned as a stress task. In this study, we found increased heart rate (Figure 3) and cortisol level (Figure 4) in participants experiencing cybersickness. We believe that cybersickness is accompanied by stress, and heart rate increases due to the accompanying stress, which confirms the findings of previous studies. In general, it is widely known that blood pressure (Figure 5) increases as heart rate increases. However, in our study, blood pressure decreased when heart rate increased. This is because the central nervous system causes a blood pressure response [3-6] since motion sickness is an abnormal adaptation of the autonomic nervous system due to the discordance between the vestibular sense and visual perception in the central nervous system [44,45]. Therefore, we believe that the change in blood pressure that is caused by cybersickness is different from the general correlation between heart rate and blood pressure. In summary, we found that the physiological responses that can be objectively measured to indicate cybersickness are heart rate and cortisol level.

**Limitations**

The number of participants (n=16) was too small to generalize the physiological responses statistically, even though they were appropriate for detecting physiological responses to cybersickness. Cybersickness is known to be sensitive to gender, age, and VR adaptation (number of experiences). However, this study did not consider these variables because our purpose was to find the physiological responses that can measure cybersickness objectively among various physiological responses. Subsequent studies should consider the number of experiences, gender, age, and VR adaptation of participants in addition to the physiological responses that were found in this study.

**Conclusions**

We analyzed the effects of cybersickness caused by HMD-based VR content on physiological responses. Heart rate, body temperature, cortisol level, and blood pressure were measured to analyze SSQ scores and physiological responses. A total of 16 participants watched the HMD-based VR content in a seated position and without moving to ensure their concentration was only on watching the VR content, which was developed to intentionally cause cybersickness.

From the results of our analysis, the following conclusions were drawn: (1) cybersickness causes significant disorientation, and research on cybersickness should focus on factors that affect disorientation; and (2) the physiological responses that are suitable for measuring cybersickness are heart rate and cortisol. This means that heart rate and cortisol level can be used as real-time factors to objectively assess cybersickness.

**Acknowledgments**

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**Data Availability**

All data generated or analyzed during this study are included in this published article.

**Conflicts of Interest**

None declared.

**References**

https://games.jmir.org/2022/4/e37938


39. Cheonan Medical Center. URL: https://www.camc.or.kr/ [accessed 2022-09-27]


42. SPSS software. IBM Corporation. URL: https://www.ibm.com/analytics/spss-statistics-software [accessed 2022-09-27]


**Abbreviations**

- **HMD**: head-mounted display
- **MIMS**: motion-induced motion sickness
- **MSAQ**: Motion Sickness Assessment Questionnaire
- **SSQ**: Simulator Sickness Questionnaire
- **VIMS**: visually induced motion sickness
- **VR**: virtual reality

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Pain Assessment Using Virtual Reality Facemask During Bone Marrow Aspiration: Prospective Study Including Propensity-Matched Analysis

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Abstract

Background: Bone marrow aspiration (BMA) is a medical procedure necessary to the diagnosis and monitoring of patients with hematological or nonhematological disorders. This procedure is considered painful, and patients are generally anxious before and during BMA.

Objective: This study assesses the effect of immersive virtual reality on pain during BMA.

Methods: This observational prospective and monocentric study enrolled 105 consecutive patients who underwent sternal BMA with lidocaine anesthesia. The study was carried on during 2 periods. First, virtual reality facemask (VRF) was proposed to all patients in the absence of exclusion criteria. During the second period, BMA was performed without the VRF. For all patients, pain intensity after the procedure was assessed using a 10-point numerical pain rating scale (NPRS). All analyses were performed on propensity score–matched cohort (with or without VRF) to evaluate efficacy on NPRS levels.

Results: The final matched cohort included 12 patients in the VRF group and 24 in the control group. No difference in anxiety level before BMA evaluated by the patient and by the operator was observed between groups (P=.71 and .42 respectively). No difference of NPRS was observed using VRF when compared to control group (median NPRS 3.8, IQR 2.0-6.3 vs 3.0, IQR 1.9-3.0, respectively; P=.09).

Conclusions: Our study did not prove the efficacy of VRF to reduce pain during BMA.

(JMIR Serious Games 2022;10(4):e33221) doi:10.2196/33221
Introduction

Bone marrow aspiration (BMA) is a standard procedure for diagnosis, staging, prognosis, and follow-up response to treatment of numerous hematologic and some nonhematologic diseases. BMA is generally carried out in adult patients without general anesthesia [1] and may be performed at different puncture sites. In France, the most common site of aspiration in adults [2] is the sternal manubrium because it is more accessible than iliac crest and may be safely performed in patients receiving anticoagulant treatment. Whatever the site of aspiration, BMA is still considered a painful procedure, and standardization of pain prevention remains a major issue. Moreover, the increase in anxiety in a clinical environment can worsen the perception of pain [3]. In a previous study, we showed that despite local anesthesia, pain scores obtained using a numerical pain rating scale (NPRS) still ranged between 2.8 and 3.5 [4]. Whatever the puncture site, the patient needs to be reassured and well informed regarding the BMA procedure to decrease anxiety and pain. Indeed, in our previous cohort, more than half of the patients were anxious or very anxious before BMA, and anxiety was found to be a major predictor of pain during the procedure. The aim of this study was to explore the effects of immersive virtual reality on BMA-associated pain scores. Indeed, this technique uses multisensory stimulation to provoke patient’s immersion in a virtual environment and a state of hypnosis, which is used to facilitate anxiolysis and analgesia during some procedures [5]. Many studies demonstrated a significant reduction in pain or a reduction in procedural anxiety [6] using a virtual reality facemask (VRF). Therefore, we conducted an observational prospective and monocentric study to compare the effects of VRF on anxiety and pain in patients undergoing sternal BMA with lidocaine anesthesia.

Methods

Ethics Approval

All the patients included were informed of the research protocol by letter, allowing them to express their opposition to the use of their data, according to French legislation and the institutional review board. The study was performed in accordance with the Declaration of Helsinki and authorized by the French Data Protection Agency (CNIL-1922081), and each patient signed consent.

Overview

This observational prospective and monocentric study enrolled consecutive patients who underwent sternal BMA with 1% lidocaine anesthesia for all patients and assessed pain during this procedure. All adult patients requiring sternal BMA between December 2019 and December 2020 were enrolled at the University Hôpital Européen Georges Pompidou (Assistance Publique-Hôpitaux de Paris, France).

The study was conducted during 2 periods. During the first period, immersive virtual reality using VRF was proposed to all patients (Figure 1). The VRF medical device was an Oculus Go helmet (Healthy Mind) consisting in a 3D video and audio headset, associated with virtual reality software. Patients were offered to choose 1 out of 3 relaxing environments (Zen garden, forest, or beach). During the second period, BMA was performed without VRF. Indeed, the COVID-19 pandemic did not allow us to use the VRF because of the risk of SARS-CoV-2 infection between patients. For both study periods, exclusion criteria were patient refusal, cognitive disorders, deep sedation, or language barrier. Patients were also excluded if they received any pharmacologic type of premedication or forms of analgesia other than subcutaneous lidocaine, such as a patch of local anesthetic or if they were offered to inhale nitrous oxide/oxygen gas premix (50%/50%).

For all patients, the same questionnaire was used, as previously described [4]. Briefly, this questionnaire included the following two assessments: (1) assessment of pain intensity following the procedurepatients were asked to quantify their pain intensity during BMA using a 10-point NPRS for which a score of 0 indicates no pain and a score of 10 indicates the worst imaginable pain; and (2) assessment of the patient’s anxiety before the procedurepatients were classified as nonanxious, anxious, or very anxious, both according to themselves and by the operator.
Figure 1. Patient wearing virtual reality facemask during sternal bone marrow aspiration.

**Statistical Analysis**

Since it has been reported in the literature that age and sex influence pain level during BMA [7-9], and to reduce confounding biases, we used propensity score method based on logistic regression to match patients with VRF with patients without VRF on sex and age using a 1:2 ratio. The matching created a balanced data set allowing comparison. In univariate analysis, continuous and categorical data were respectively expressed as median IQR (25th to 75th percentile) and as frequencies and percentages and compared using Mann-Whitney-Wilcoxon test and Fisher exact test. Statistical analysis was performed using R studio software, including R version 3.6.3 (R Development Core Team).

**Results**

From December 2019 to December 2020, a total of 105 patients were enrolled (Figure 2). Of these, 19 (18.1%) patients fulfilling the exclusion criteria as well as 17 (16.1%) patients who underwent an iliac crest aspiration were excluded; 1 (1%) patient who removed the mask during procedure was excluded (failure of the procedure), and pain level was not evaluable after procedure. Finally, after age and sex matching, the final cohort included 36 patients, 24 (67%) without VRF (control group) and 12 (33%) wearing a VRF (VRF study group) during BMA. Patient’s characteristics, BMA indication, and final diagnosis for all patients in the matched cohort are presented in Table 1. Briefly, the median age of patients was 66.7 (IQR: 59.4-76.2) years. More than half of the BMAs were conducted in patients from the internal medicine department (9/36, 25%), from the nephrology department (7/36, 19%), or oncology department (7/36, 19%). Regarding the indication, 15 BMAs (42%) were performed to explore a monoclonal gammapathy, 8 (22%) for an isolated nonregenerative anemia, and 8 (22%) for a bicytopenia or a pancytopenia. Groups did not significantly differ in terms of BMA indication or diagnosis. No complications related to the procedure were recorded.

Among the various relaxing environments, 8 (66%) patients of the VRF group chose the beach, 2 (17%) the forest, and 2 (17%) Zen garden videos. Importantly, the total immersion time recorded in the VRF group was estimated at 15 minutes (IQR 12-15).

Before procedure, anxiety level did not differ between groups, regardless of whoever assessed this parameter (the patient himself or the operator). Thus, in the control group 10/24 (41.7%) patients were considered anxious, and 6/24 (25%) were considered very anxious compared to the 5/12 (41.7%) anxious and 1/12 (8.3%) very anxious patients in the VRF group ($P=.71$). When the patient himself evaluated anxiety level, in the control group 10/24 (45.5%) patients were anxious and 2/24 (9.1%) were very anxious, compared to the 4/12 (33.3%) anxious and 2/12 (16.7%) very anxious patients in VRF group ($P=.42$).

Concerning BMA-associated pain, no difference in NPRS was observed between groups (median NPRS 3.8, IQR 2.0-6.3 vs 3.0, IQR 1.9-3.0; $P=.09$), for the VRF and the control group, respectively.)
Figure 2. Patient flowchart. VRF: virtual reality facemask. BMA: bone marrow aspiration. *reasons for declining were for the first patient a noninterest by this technology and for the second patient a desire to see the gesture and not be distracted by virtual reality.
Table 1. Patient’s characteristic, bone marrow aspiration (BMA) indication, and outcomes between wearing a virtual reality mask and not wearing a virtual reality mask during BMA (N=36).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Matched cohort</th>
<th>VRF(^a) group (n=12)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control group (n=24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years), median (IQR)</td>
<td>66.4 (60.2-75.1)</td>
<td>66.7 (59.1-76.4)</td>
<td>.80</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td>.99</td>
</tr>
<tr>
<td>Female</td>
<td>11 (46)</td>
<td>6 (50)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13 (54)</td>
<td>6 (50)</td>
<td></td>
</tr>
<tr>
<td>Clinical department, n (%)</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>5 (21)</td>
<td>4 (33)</td>
<td></td>
</tr>
<tr>
<td>Nephrology</td>
<td>5 (21)</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>Oncology</td>
<td>4 (17)</td>
<td>3 (25)</td>
<td></td>
</tr>
<tr>
<td>Geriatrics</td>
<td>2 (8)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Hematology outpatients</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Surgery units</td>
<td>1 (4)</td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>Other departments</td>
<td>6 (25)</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>BMA indication, n (%)</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Suspcion monoclonal gammopathy</td>
<td>10 (42)</td>
<td>5 (42)</td>
<td></td>
</tr>
<tr>
<td>Bicytopenia or pancytopenia</td>
<td>7 (29)</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>Isolated nonregenerative anemia</td>
<td>5 (21)</td>
<td>3 (25)</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>1 (4)</td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Suspcion metastasic tumors</td>
<td>0 (0)</td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>Anxiety level assessed by the operator (%)</td>
<td></td>
<td></td>
<td>.42</td>
</tr>
<tr>
<td>Nonanxious</td>
<td>8 (33)</td>
<td>6 (50)</td>
<td></td>
</tr>
<tr>
<td>Anxious</td>
<td>10 (42)</td>
<td>5 (42)</td>
<td></td>
</tr>
<tr>
<td>Very anxious</td>
<td>6 (25)</td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>Anxiety level assessed by the patient (%)</td>
<td></td>
<td></td>
<td>.71</td>
</tr>
<tr>
<td>Nonanxious</td>
<td>10 (46)</td>
<td>6 (50)</td>
<td></td>
</tr>
<tr>
<td>Anxious</td>
<td>10 (46)</td>
<td>4 (33)</td>
<td></td>
</tr>
<tr>
<td>Very anxious</td>
<td>2 (9)</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>NPRS(^b) score, median (IQR)</td>
<td>3.0 (1.9-3.0)</td>
<td>3.75 (2.0-6.3)</td>
<td>.09</td>
</tr>
<tr>
<td>Immersion video, n (%)</td>
<td></td>
<td></td>
<td>N/A(^c)</td>
</tr>
<tr>
<td>Forest</td>
<td>0 (0)</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>Zen garden</td>
<td>0 (0)</td>
<td>2 (17)</td>
<td></td>
</tr>
<tr>
<td>Beach</td>
<td>0 (0)</td>
<td>8 (66)</td>
<td></td>
</tr>
<tr>
<td>Immersion time, median (IQR)</td>
<td>N/A</td>
<td>15.00 (12.0-15.0)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

\(^a\)VRF: virtual reality facemask.

\(^b\)NPRS: numerical rating scale score.

\(^c\)N/A: not available.
Discussion

Principal Findings

To the best of our knowledge, this study is the first using VRF to try to reduce anxiety and pain during BMA. We did not observe any benefit of the VRF on anxiety levels before or during BMA and pain scores following BMA. We previously showed [4] that a greater level of anxiety before the procedure in patients leads to a greater sensation of pain during BMA as evaluated by the NPRS after the procedure. In this study, the VRF had no significant impact on anxiety or pain. A strength of this prospective study is that preprocedure anxiety levels were not significantly different between the two groups. Therefore, anxiety level did not impact pain assessment as we previously described [4].

The median immersion time with VRF was 15 minutes. Thus, the use of VRF could increase procedure duration, owing to the need to provide explanations to the patient and to the various manipulations for device placement and cleaning. Contrary to our findings, several studies using virtual reality therapy showed positive results in terms of reduction of pain and anxiety during medical procedures [6]. It must be mentioned that results might differ according to patient populations and indications [6].

Limitations

We acknowledge some limitations. First, the COVID-19 pandemic resulted in a premature arrest of the study, given the risk of contamination between patients using facemask, thus explaining the low number of participants in the VRF group. Therefore, a larger scale and randomized study is needed to confirm our results. Second, sternal BMA is far from being the most common puncture site used worldwide [1]. However, the sternal site is often chosen when BMA is not associated with a bone marrow biopsy. In this study, no complications related to the BMA procedure were recorded [4]. The supine position is far easier for using VRF compared with prone decubitus, which is why our study is focused on sternal BMA. Further studies need to confirm these results for iliac BMA. Third, we acknowledge that anxiety was not assessed with predefined criteria but according to the operator and the patient, as the main objective of this study was the evaluation of VRF on pain. We chose to evaluate anxiety according to our previous paper [4] to allow easier comparison of our results where anxiety was found to be a major predictor of pain during the procedure.

Finally, our cohort included only patients who did not have any BMA previously, which probably explains why patients were usually anxious about this procedure. It would be interesting to conduct a similar study on patients undergoing repeated BMA for chronic malignant hematology disease to see if the technique proves more helpful in this setting.

Conclusion

This study did not detect any benefit associated with the use of an immersive virtual reality to reduce pain and anxiety associated with sternal BMA in addition to local anesthesia.

Conflicts of Interest

None declared.

References

Correction: Development of a Therapeutic Video Game With the MDA Framework to Decrease Anxiety in Preschool-Aged Children With Acute Lymphoblastic Leukemia: Mixed Methods Approach

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Related Article:
Correction of: https://games.jmir.org/2022/3/e37079
doi:10.2196/43211

In “Development of a Therapeutic Video Game With the MDA Framework to Decrease Anxiety in Preschool-Aged Children With Acute Lymphoblastic Leukemia: Mixed Methods Approach” (JMIR Serious Games 2022;10(3):e37079) the authors noted a few errors in Table 3.

In the originally published paper, the headings of subcolumns appeared as “FRS score, range” and “FRS score, mean (SD).” These headings have been corrected to “Range” and “Mean (SD),” respectively. The sequence of footnotes was revised accordingly. The updated version of Table 3 can be viewed below. The originally published Table 3 is in Multimedia Appendix 1.
Table 3. Caregiver-reported invasive therapies.

<table>
<thead>
<tr>
<th>Invasive therapy administered</th>
<th>Experimental group (n=7)</th>
<th>Control group (n=8)</th>
<th>P value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Times administered, n (%)</td>
<td>Range</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>IM&lt;sup&gt;b&lt;/sup&gt; injection (buttocks injection)</td>
<td>25 (37)</td>
<td>1-5</td>
<td>3.5 (1.6)</td>
</tr>
<tr>
<td>PORT&lt;sup&gt;c&lt;/sup&gt; puncture</td>
<td>17 (25)</td>
<td>0-6</td>
<td>2.8 (1.9)</td>
</tr>
<tr>
<td>IV&lt;sup&gt;d&lt;/sup&gt; injection</td>
<td>13 (19)</td>
<td>1-6</td>
<td>1.9 (1.9)</td>
</tr>
<tr>
<td>IT&lt;sup&gt;e&lt;/sup&gt; injection</td>
<td>6 (9)</td>
<td>0-2</td>
<td>2 (0)</td>
</tr>
<tr>
<td>BMA&lt;sup&gt;f&lt;/sup&gt;</td>
<td>4 (6)</td>
<td>0-2</td>
<td>2 (0)</td>
</tr>
<tr>
<td>BT&lt;sup&gt;g&lt;/sup&gt;</td>
<td>2 (3)</td>
<td>0-2</td>
<td>2 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>67 (100)</td>
<td>6-15</td>
<td>9.6 (3.5)</td>
</tr>
</tbody>
</table>

<sup>a</sup>This P value was based on the Mann-Whitney U test.
<sup>b</sup>IM: intramuscular.
<sup>c</sup>PORT: port-a-cath catheter system.
<sup>d</sup>IV: intravenous.
<sup>e</sup>IT: intrathecal.
<sup>f</sup>BMA: bone marrow aspiration.
<sup>g</sup>BT: blood transfusion.

The correction will appear in the online version of the paper on the JMIR Publications website on October 5, 2022, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.